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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/092,926	NGUYEN ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *24-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23,36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed May 13, 2005 is acknowledged and has been entered.

Election/Restrictions

Applicant's arguments directed to the amendment to claim 1 incorporating the limitations of claim 36 are found persuasive and therefore, Group III claims 36 and 37 are rejoined with Group I. However, the restriction of Group II is maintained because the kit could be used with a materially different process such as cell separation or purification processes. Thus claims 1-37 are pending. Claims 24-35 are withdrawn from consideration.

Specification

1. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 36 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36 is vague and indefinite because the preamble of the claim does not correlate with the body of the claim. The preamble of the claim recites "analyzing a sample for a plurality of modified proteins. However, the body of the claim does not positively recite analyzing a sample for a plurality of modified proteins.

Claim 36 the recitation "in a process" is vague and indefinite. It is unclear what process Applicant is referring to.

Claim 36, line 2 the recitation "the step of denaturing modified proteins" there is insufficient antecedent basis for this limitation.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 3-16 and 21-23, 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shen et al (US 2003/0153014) in view of Knowles et al (US 4,658,022).

Shen et al disclose methods for determining a plurality of modified proteins in a sample simultaneously. Shen et al disclose contacting the sample with a plurality of antibodies (first antibodies) immobilized on a solid support (page 2) in the form of an array (page 3, 16 and figures 1-2). Shen et al disclose performing wash steps to remove unbound materials from the first antibodies (p. 16, paragraph 0171). Shen et al disclose adding modification specific detection antibodies (second antibodies) to detect the modified proteins in the sample. Shen et al disclose that the modified proteins can be phosphorylated, (p. 2, paragraph 0016). Shen et al disclose the solid support can be sets of beads (particles) (p. 2, paragraph 0015). Shen et al disclose that the beads can be tagged. Shen et al disclose that the tag can be color, fluorescence, oligo,

radiofrequency tage and other tag that can be easily used to separate beads with different tags (paragraph 0171). Shen et al disclose that the solid support can be made of glass or polystyrene (paragraph 0156). Shen et al disclose the solid support material can be a slide or a chip (paragraph 0015). Shen et al disclose that the protein can be p38 MAP kinase. Shen et al disclose that the second antibodies can be biotinylated (paragraph 0171).

Shen et al differ from the instant invention in failing to teach contacting the sample under mild protein denaturation conditions with the first antibodies.

Knowles et al disclose methods for the detection of modified proteins. Knowles et al disclose contacting the sample to denaturing conditions with immobilized antibodies. Knowles et al disclose that the denaturing agent can be sodium dodecylsulfate (col. 8) (same agent applicant is using). Knowles et al disclose that the temperature can be performed at 37 degrees C or less and at a time of one to several hours. Knowles et al also disclose diluting the concentration to less than about 1.0 molar. Knowles et al disclose that denaturation effectively exposes or enhances the exposure of the linear peptide epitope or binding by the antibody reagent (abstract) and that it provides a general approach to improving the specificity of binding and detection of proteins of analytical interest such as in medical diagnostics (col 9, lines 20-24) and thus is particularly useful in performing immunoassays (abstract).

It would have been obvious to one of ordinary skill in the art to incorporate denaturation conditions and agents such as taught by Knowles et al into the method of Shen et al because Knowles et al teaches that denaturation effectively exposes or

enhances the exposure of the linear peptide epitope or binding by the antibody reagent (abstract) and that it provides a general approach to improving the specificity of binding and detection of proteins of analytical interest such as in medical diagnostics (col 9, lines 20-24) and thus is particularly useful in performing immunoassays.

With respect to the concentration, temperature and time ranges as recited in the instant claims. The optimum concentration, temperature and time ranges may be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

8. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shen et al and Knowles et al in view of Chin et al (US 6,197,599).

See above for teachings of Shen et al and Knowles et al.

Shen et al and Knowles et al differ from the instant invention in failing to teach wherein up to 100 modified proteins are detected.

Chin et al disclose arrays of immobilized antibodies for detecting analytes of interest. Chin et al disclose that the arrays can have thousands of different antibodies immobilized on a solid support (col 4). Chin et al disclose that this provides a powerful and quantitative tool for determining posttranslational modifications and provides a valuable tool to investigate protein and cellular regulations.

It would have been obvious to one of ordinary skill in the art to incorporate arrays as taught by Chin et al into the modified method of Shen et al because Chin et al teaches that this provides a powerful and quantitative tool for determining posttranslational modifications and provides a valuable tool to investigate protein and cellular regulations. Further, the number of 100 modified proteins as recited in the instant claims can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

9. Claims 17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shen et al and Knowles et al in view of Bayer et al., (Immunoassay, edited by Diamandis et al., The Avidin-Biotin System, Chapter 11, p. 237-267).

See above for teachings of Shen et al and Knowles et al.

Shen et al and Knowles et al differ from the instant invention in failing to teach contacting the product of step (c) with a labeled moiety.

Bayer et al disclose the use of the avidin-biotin system in immunoassay. Bayer et al disclose biotinylated antibodies which are detected by avidin-probe conjugates (labeled moiety) (p. 257-258). Bayer et al disclose several advantages of the avidin-biotin system. Bayer et al disclose that the avidin-biotin system greatly improves performance if the immunoassay and improves the characteristics of the capture system (p. 237) and that there is more control over the immobilization procedure, since the amount of immunochemically active antibody molecules applied to the solid phase can be more precisely regulated (p. 255).

It would have been obvious to one of ordinary skill in the art to incorporate avidin-biotin system into the modified method of Shen et al because Shen et al specifically teaches that the second antibody can be biotinylated and further because Bayer et al shows that this avidin-biotin system greatly improves performance if the immunoassay and improves the characteristics of the capture system and that there is more control over the immobilization procedure, since the amount of immunochemically active antibody molecules applied to the solid phase can be more precisely regulated

10. Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shen et al and Knowles et al in view of Bayer et al as applied to claims 1, 3-17 and 20-23 above, and further in view of Roser (US 4,891,319).

See above for teachings of Shen et al., Knowles et al., and Bayer et al.

Shen et al., Knowles et al., and Bayer et al differ from the instant invention in failing to teach the labeled moiety comprises a phycoerythrin.

Roser teaches phycoerythrin Avidin/Streptavidin conjugate used in fluorescent assays (col 4, lines 43-54). Roser teaches that this fluorescent protein is 20 times brighter than fluorescein on a molar basis and can easily be coupled to probes.

It would have been obvious to incorporate phycoerythrin conjugates as taught by Roser into the modified method of Shen et al because Roser teaches that this fluorescent protein is 20 times brighter than fluorescein on a molar basis and can easily be coupled to probes.

Response to Arguments

11. Applicant's arguments filed May 13, 2005 have been fully considered but they are not persuasive.

Applicant argues that the denaturation conditions of the current application as compared to Knowles et al., a lower concentration of sulfate or sulfonate detergent (about 1-10mM as opposed to 1-3 molar), a lower temperature of between about 4 and about 37 degrees C (as opposed to 50 degrees C and higher), and for a time of from about 2 to about 72 hours (as opposed to about 1 minute). This is not found persuasive because as stated above Knowles also teaches that the temperature can be performed at 37 degrees C or less and at a time of one to several hours. Knowles et al also disclose diluting the concentration to less than about 1.0 molar. Further as stated above the optimum temperature, time and concentration can be determined by routine experimentation.

Applicant further argues that the specification teaches that a sulfonate detergent such as SDS can be effectively used for protein denaturation under such comparatively mild conditions is surprising. This is not found persuasive because a showing of unexpected results must be based on evidence, not argument or speculation. *In re Mayne* 104 F.3d 1339, 1343-44, 41 USPQ 2d 1451, 1455-56 (FED Cir. 197). Further, the Applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range. *In re Woodruff,* 919 F.2d 1575, 16 USPQ2d 1934 (Fed cir. 1990).

Applicant argues that the tertiary references (Chin et al., Bayer. And Roser) fail to disclose protein denaturation so fails to fill the gap left by the combination of Shen et al and Knowles et al. This is not found persuasive because the Examiner has not relied upon the tertiary references for these teachings but rather has relied upon the combination of Shen et al and Knowles et al for this limitation. Therefore, the Examiner maintains that the combination of the tertiary references with Shen et al and Knowles et al is appropriate and reads on the instantly recited clams.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
July 1, 2005

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07/05/05